

**Amendments to the Specification:**

Please replace the paragraph at lines 13-22 of page 1, with the following rewritten paragraph:

The tumor-associated antigen MUC1 is a high-molecular weight glycoprotein that is expressed on many adenocarcinomas. Gendler, *et al*, J.Biol. Chem. 265:15286, 1990, Gendler *et al.*, P.N.A.S. U.S.A., 84:6060, 1987, Siddiqui, *et al.*, Proc. Natl. Acad. Sci. U.S.A. 85:2320, 1988, and Lightenberg, *et al.*, J. Biol. Chem. 265:5573, 1990 teach that the extracellular domain of the integral membrane glycoprotein consists mainly of 30 to 90 tandem repeats of a 20 amino acid core sequence that is rich in serine, threonine and praline, GSAPPAHGVTSAPDTRPAP (SEQ ID NO: 1). Burchell, *et al.*, Cancer Surv. 18:135, 1993, teaches that the number of repeats expressed by an individual is genetically determined, resulting in size polymorphism.

Please replace the paragraph at lines 23-31 of page 1, with the following rewritten paragraph:

Price, *et al.* Breast 2:3, 1993, teaches that the minimum sequence recognition of most MUC1 reactive monoclonal antibodies all lie within APDTRPAP (SEQ ID NO: 2), which is believed to be a type 1 $\beta$ -turn. Burchell, *et al.* Cancer Surv. 18:135, 1993, discloses that the sequence SAPDTRP (SEQ ID NO: 3) in the MUC1 tandem repeat is an immunodominant B cell epitope and the at a T cell epitope of the tandem repeat has been mapped to the pentamer, PDTRP (SEQ ID NO: 4). Adjacent amino acids and sugar residues may play an important role in the binding in the native molecule. A large number of tandem repeats may be present in the MUC1 mucin, ranging between 30 and 90 per molecule.

Please replace the paragraph at lines 22-24 of page 7, with the following rewritten paragraph:

Figures 7A-1 through 7A-8 are a series of bar graphs showing the inhibition of anti-MUC1 antibody positive patients samples with MUC1-derived peptides (SEQ ID NOS: 5-9), where the patient samples are not pre-treated.

Please replace the paragraph at lines 25-26 of page 7, with the following rewritten paragraph:

Figures 7A-9 is a bar graph showing inhibition of binding to the 31-mer by the positive control antibody, Alt-1, with the indicated peptides (SEQ ID NOS: 5-9).

Please replace the paragraph at lines 29-30 of page 7 and lines 1-2 of page 8, with the following rewritten paragraph:

Figures 7B-8 are a series of bar graphs showing the inhibition of anti-MUC1 antibody positive patient samples with MUC1-derived peptides (SEQ ID NOS: 5-9), where the patient samples are pre-treated to disrupt MUC-1/anti-MUC-1 immune complexes.

Please replace the paragraph at lines 14-26 of page 10, with the following rewritten paragraph:

In preferred embodiments, the binding agent binds an epitope that comprises immunological determinants from amino acid residues of a peptide having the amino acid sequence DTRPAP (SEQ ID NO: 5). An "amino acid residue" is an amino acid as it is in place in a particular peptide. "Inhibition of biological activity", as used herein, means a statically significant reduction in tumor burden, or a statistically significant prolongation of survival in an animal or patient bearing a tumor. Such statistically significant inhibition is illustrated in the examples hereof. Certain preferred embodiments of binding agents according to the invention are non-radiolabeled. Certain binding agents according to the invention bind to both circulating and tumor-bound tumor-associated MUC-1, wherein "tumor-associated" refers to the altered glycosylation of MUC-1 made by tumor cells, rather than to its proximity to a tumor. A particularly preferred binding agents is Alt-1 (ATFCC Patent Deposit Designation PTA-975).

Please replace the paragraph at lines 27-29 of page 10 to lines 1-4 of page 11, with the following rewritten paragraph:

Preferred tumors for treatment include, without limitation, breast carcinoma, colon carcinoma, esophageal squamous cell carcinoma, pancreatic carcinoma, prostate carcinoma and multiple myeloma molecular weight glycoprotein that is expressed on many tumors (Ho *et al.* Cancer Res. 53:641, 1993). The binding agent specifically recognizes the sequence DTRPAP (SEQ ID NO: 5) within the MUC1 tandem repeat peptide sequence. This binding agent is referred to as Alt-1.

Please replace the paragraph at lines 25-31 of page 40, with the following rewritten paragraph:

The samples were mixed with various MUC1 derived peptides and pre-incubated for 30 to 60 min. The mixture was assayed in the anti-MUC1 antibody assay. The amount of detected antibody was compared to serum with no additional peptide to determine which peptides caused an inhibition of binding of antibody by competing with the coated MUC1 peptide (E31-biotin, sequence APDTRPAPGSTAPPAHGVTSAPDTRPAPGSC (SEQ ID NO: 11)). The following peptides were used: E31, DTRPAP (SEQ ID NO: 5), APGSTA (SEQ ID NO: 6), TAPPAH (SEQ ID NO: 7), AHGVTS (SEQ ID NO: 8), and TSAPDT (SEQ ID NO: 9).

Please replace the paragraph at lines 1-6 of page 41, with the following rewritten paragraph:

Alt-1 with known epitope specificity was used as a control (see Figure 7A-9). As can be seen in the Figure 7A-9, only the 31-mer (E31) MUC1 peptide (as used for coating of the plates) and the DPRPAP (SEQ ID NO: 5) peptide inhibited the binding of Alt-1. These results are consistent with the previously determined epitope specificity of MAb-AR20.5, delineating the minimum MUC1 epitope recognized by Alt-1 as DTRPAP (SEQ ID NO: 5).

Please replace the paragraph at lines 7-20 of page 41, with the following rewritten paragraph:

As can be seen in Figures 7A and 7B, various inhibition patterns were present from patient to patient. IN some cases there was also a shift of recognized epitopes over time. In

pretreated (Figure 7B) as well as untreated serum samples (Figure 7A), the epitope recognized by most patients was represented by the peptide AHGVTS (SEQ ID NO: 8) (8 of 15 samples). Peptides APGSTA (SEQ ID NO: 6) and TAPPAH (SEQ ID NO: 7) were also frequently recognized using untreated serum (6 or 5 or 15 samples, respectively). Peptides TSAPDT (SEQ ID NO: 9), APGSTA (SEQ ID NO: 6), and TAPPAH (SEQ ID NO: 7) were frequently recognized using pretreated serum samples (5,4 and 4 of 15 samples, respectively). The epitope represented by peptide DTRAPA (SEQ ID NO: 5) was recognized in only 3 (untreated) or 1 (treated) of 15 samples. Serum samples from 3 patients produced antibodies to MUC1 that were restricted to a single 6-mer region (AHGVTS (SEQ ID NO: 8) in two cases and APCSTA (SEQ ID NO: 6) or TAPPAH (SEQ ID NO: 7) in one case.) The remaining patients developed a multi-epitomic response, covering most of the tested epitopes. It is interesting to note, that the DTRPAP (SEQ ID NO: 5) epitope was recognized the weakest.

Please replace the paragraph at lines 21-27 of page 41, with the following rewritten paragraph:

Thus, samples from patients treated with Alt-1 and were positive for anti-MUC-1 antibodies, antibodies that could be blocking from binding to MUC-1 by various peptides are shown in Figures 7A and 7B. These results demonstrate that human antibodies bind epitopes DTRPAP (SEQ ID NO: 5), APGSTA (SEQ ID NO: 6), TTTAPPAH (SEQ ID NO: 10), AHGVTS (SEQ ID NO: 8), and TSAPDT (SEQ ID NO: 9). These results demonstrate that a multi-epitopic immune response is elicited by the administration of a single TSA-specific murine monoclonal antibody, in this case Alt-1.

Please replace the paragraph at lines 25-31 of page 41 and 1-7 of page 42, with the following rewritten paragraph:

In summary, human anti-MUC1 antibodies, induced after injection of Alt-1, recognized multiple epitopes. In both experimental set-ups, the epitope of AHGVTS was recognized predominantly. In the literature, naturally occurring antibodies to MUC1 were mainly directed to the PDTRP (SEQ ID NO: 4) region of MUC1. These results indicate that the MUC1 mucin is

differently processed if taken up in complex with Alt-1. These results also indicate that the majority of human anti-MUC1 antibodies in patients treated with Alt-1 were not induced via the idiotypic network (Ab3 by definition would bind to the same epitope as the Ab1, *i.e.*, DTRPAP (SEQ ID NO: 5)) but rather via complex formation with circulating tumor-derived MUC1.